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FILE

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SCIENTIFIC DATA REVIEWS
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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

25-MAR-1999

SUBJECT: PP#8F05022. Pyriproxyfen in/on Citrus, Fruiting Vegetables, and Tree Nuts. Evaluation of Residue Data and Analytical Methods. Chemical # 129032. DP Barcode D253836. Case 290406. Submission S548311. MRID #s 44630102 thru 44630107, and 44638301.

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The following is a review of pyriproxyfen residue chemistry data submitted in support of a Section 3 permanent registration for citrus, fruiting vegetables, and tree nuts. The initial review was conducted by Dynamac under the supervision of HED. The Dynamac review has undergone secondary review in RAB1 and has been revised to reflect current policies and decisions.

Executive Summary of Chemistry Deficiencies

- Revised KNACK™ and ESTEEM™ labels with specification of ground or aerial application equipment clearly indicated under Special Instructions for each pest use for almond and citrus, as well as the quantity of spray oil that may be added to the final spray volume. In addition, the labels should specify minimum retreatment intervals for each crop.

- Revised Section B specifying a 30-day plantback interval as a rotational crop restriction for fruiting vegetables.

- Revised Section F specifying tolerance levels of 0.2 and 2.0 ppm for fruiting vegetables and citrus pulp, dried, respectively.

- Successful completion of Agency analytical method validation for citrus, fruiting vegetables, and almonds.

- Data from 5 pecan crop field trials to support the proposed tree nut crop group tolerance.

INTRODUCTION

Valent USA Corporation has submitted a petition for the establishment of permanent tolerances for residues of the insecticide pyriproxyfen in/on citrus fruits, fruiting vegetables, and tree nuts. The petitioner is proposing the establishment of permanent tolerances for residues of pyriproxyfen *per se* as follows:

Citrus Fruits	0.3 ppm
Fruiting Vegetables (Except Cucurbits)	0.1 ppm
Tree Nuts	0.02 ppm
Almond Hulls	2.0 ppm
Citrus Oil	20.0 ppm
Citrus Pulp, Dried	1.5 ppm

Pyriproxyfen [2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy]pyridine] is an analogue of an insect juvenile hormone and interferes with the hormonal control of insect growth and development, thereby inhibiting egg hatch, larval embryogenesis, metamorphosis, and adult emergence. Pyriproxyfen is proposed for use in controlling various insect pests such as scale, citrus whitefly, citrus leafminer, citrus blackfly, silverleaf whitefly, and sweet potato whitefly.

Permanent tolerances for pyriproxyfen have been established under 40 CFR §180.534 at 0.05 and 2.0 ppm in/on cotton seed and cotton gin byproducts, respectively (PP#6F04737, DP Barcodes D241303 & D228499, W. Donovan, W. Dykstra, and B. Tarplee, 27-FEB-1998). In addition, permanent tolerances for residues in/on pome fruits, walnuts, and wet apple pomace are pending resolution of deficiencies pertaining to analytical methodology and product labels (PP#7F04882, DP Barcode D238190, W. Donovan, 07-DEC-1998). Prior to the cotton petition, pyriproxyfen was registered for only non-food uses. Based on plant metabolism studies conducted on cotton, apples, and tomatoes, the HED Metabolism Assessment Review Committee (MARC) determined that the residue of concern in plants is pyriproxyfen *per se* (DP Barcode D250953, W. Donovan & W. Dykstra, 19-NOV-1998).

Associated with this petition are 7 volumes of residue chemistry submissions which are evaluated in this document.

CONCLUSIONS

OPPTS GLN 860.1200: Proposed Uses

1. The proposed use directions for the 0.86 and 2.9 lb ai/gal ECs are inadequate. The labels should be amended to specify a minimum retreatment interval (RTI) for each of the crops. The crop field trial data support RTIs of 21, 14, and 14 days for citrus, fruiting vegetables, and almonds, respectively. The proposed labels for almonds and citrus should be amended to specify the type of application equipment (ground or aerial equipment) allowed. In addition, for almonds and citrus, the labels should specify the quantity of spray oil that may be added to the final spray volume. A revised Section B should be submitted.

OPPTS GLN 860.1300: Nature of the Residue - Plants

2a. The tomato metabolism study is adequate. Total radioactive residues in whole fruit, calculated by summing residues in surface wash, juice and pomace were 0.265 ppm in tomatoes treated with pyridyl labeled [^{14}C]pyriproxyfen and 0.351 ppm in tomatoes treated with phenyl labeled [^{14}C]pyriproxyfen at 2x the maximum seasonal rate and harvested 7 days following the last of three applications. ^{14}C-Residues in juice accounted for 13-32% of the whole fruit TRR, pomace contained 66-83%, and surface washes accounted for 2-3%. Nonextractable residues accounted for only ~5% TRR.

2b. The parent pyriproxyfen was the major component of the residue, accounting for 50-68% of the TRR. Related metabolites were present in free and conjugated forms. PYPA (sum of free and bound forms) comprised 10.9% of the residue in the pyridyl labeled tomatoes. 4'-OH-PYR and DPH-PYR were formed from both labeled compounds at 5-6% and 2% TRR, respectively. In phenyl-labeled tomatoes 4'-OH-POPA and 4'-OH-POP (free and bound) accounted for 2.5 and 2% TRR and in pyridyl-labeled tomatoes PYPAC (free and bound) and 2-OH-PY (as the conjugate), respectively, accounted for 7.9 and 4.9%. The identities of parent and metabolites were determined by HPLC and confirmed by TLC and GC/MS.

2c. Based on this study, metabolism of pyriproxyfen in tomatoes proceeds by hydroxylation and cleavage of the phenoxy ether linkage. Primary metabolites formed are further metabolized to more polar products by oxidation or conjugation reactions. Similar metabolic pathways were observed for the metabolism of pyriproxyfen in apples, cotton, goats, and hens.

2d. Accordingly, the HED MARC decided that the residue of concern in plants is pyriproxyfen *per se* (DP Barcode D250953, W. Donovan & W. Dykstra, 19-NOV-1998), unless a significantly different metabolic pathway is identified for a given crop. This finding confirms the 15-JUL-1996 HED MARC decision rendered for cotton.

OPPTS GLN 860.1300: Nature of the Residue - Animals

3a. No animal metabolism data were submitted with this petition. Ruminant and poultry metabolism studies have previously been submitted and reviewed (PP#6F04737, DP Barcode D228556, J. Garbus, 06-MAY-1997) in conjunction with a petition for cotton. The animal metabolism studies demonstrated that the transfer of ^{14}C residues to tissues was low. Radioactivity in goat milk, muscle, and tissues accounted for less than 2% of the administered dose. Radioactivity in poultry eggs, muscle, and tissue accounted for ~2.7% of the administered dose.

3b. The nature of the residue in animals is adequately understood. The HED MARC determined that should future crop uses increase the maximum theoretical dietary burden to the point that tolerances are needed in animal commodities, the residue of concern will be pyriproxyfen and the free and sulfate forms of 4'-OH-PYR (D250953, W. Donovan & W. Dykstra, 19-NOV-1998).

OPPTS GLN 860.1340: Residue Analytical Methods - Plants

4a. The GC/nitrogen-phosphorous specific flame ionization detector (NPD) and HPLC/fluorescence (FLD) method RM-33P-1-3 is adequate for collecting data on residues of pyriproxyfen and 4'-OH-PYR in/on citrus fruits. Adequate method validation data have been submitted for this method. The method has been adequately radiovalidated using samples from the apple metabolism study, and has undergone a successful independent laboratory validation (ILV). The method has also been recommended for an Agency method validation in conjunction with the permanent tolerance petition for residues of pyriproxyfen in/on apples (D252371, W. Donovan, 28-JAN-1999). The limit of quantitation (LOQ) is 0.02 ppm for residues of pyriproxyfen and 4'-OH-PYR in/on citrus fruits.

4b. GC/NPD method RM-33P-9 is adequate for collecting data on residues of pyriproxyfen and PYPA in/on tomato and peppers. Adequate method validation data have been submitted for this method, which has been recommended for Agency method validation (D252371, W. Donovan, 28-JAN-1999). The LOQ is 0.02 ppm for residues of pyriproxyfen and PYPA in/on tomato and peppers.

4c. The GC/NPD and HPLC/FLD method RM-33N-2 is adequate for collecting data on residues of pyriproxyfen and 4'-OH-PYR in/on almond nutmeat. Adequate method validation data have been submitted for this method, which has been recommended for Agency method validation (D252371, W. Donovan, 28-JAN-1999). The LOQ is 0.02 ppm for residues of pyriproxyfen and 4'-OH-PYR in/on almond nutmeat.

4d. The GC/NPD and HPLC/FLD method RM-33H is adequate for collecting data on residues of pyriproxyfen and 4'-OH-PYR in/on almond hulls. Adequate method

validation data have been submitted for this method, which has been recommended for Agency method validation (D252371, W. Donovan, 28-JAN-1999). The LOQ is 0.02 ppm for residues of pyriproxyfen and 4'-OH-PYR in/on almond hulls.

4e. Because the HED MARC concluded that pyriproxyfen *per se* is the residue of concern in plant commodities, the proposed enforcement methods should be amended to remove procedures for the recovery of metabolites of pyriproxyfen (i.e., 4'-OH-PYR and PYPA).

4f. As tolerances for residues of pyriproxyfen in animal commodities are not required at this time, enforcement methodology for determining residues in animals is not required.

OPPTS GLN 860.1360: Multiresidue Method

5. Multiresidue testing data have previously been provided (PP#6F04737, DP Barcode D228556, J. Garbus, 06-MAY-1997) for pyriproxyfen and its metabolite PYPAC. Pyriproxyfen was recovered from fortified apple and cotton samples through protocols A, C, D, E, and F. The metabolite PYPAC was tested with protocols A, B, C, and D. The PAM-1 multiresidue method for pyriproxyfen (MRID 44036926) was forwarded to FDA (R.W. Cook, 24-JAN-1997).

OPPTS GLN 860.1380: Storage Stability Data

6a. The submitted storage stability data are adequate and indicate that pyriproxyfen is stable at -20°C for up to 4 months in almond hulls and oranges, and up to 3 months in peppers. Pyriproxyfen residues in tomatoes declined by ~25% within one week, and by 40-60% after 1 month of frozen storage at -20°C; however, the majority of the tomato residue samples were analyzed within one week of sampling. The maximum frozen storage interval from sampling to analysis for almond, citrus, and pepper samples was < 1-3 months. These data, together with previously submitted data indicating that residues of pyriproxyfen are stable in frozen walnut nutmeat for 3 months, adequately support the residue data submitted for the permanent tolerance petition for citrus, fruiting vegetables, and tree nuts.

6b. The submitted storage stability data, together with existing storage stability data on walnuts, indicate that residues of 4'-OH-PYR and PYPA are relatively stable in almonds and oranges, and tomato and peppers, respectively, over the storage intervals and conditions reflected in the residue studies (≤3 months at ~-20°C).

OPPTS GLN 860.1500: Crop Field Trials

7a. **Fruiting Vegetables**: The submitted field trial data on fruiting vegetables are adequate. Geographic representation of tests on peppers and tomatoes conformed to OPPTS Series 860 guidelines and an adequate number of samples were analyzed. Residues of pyriproxyfen were <0.01-0.06 ppm in/on 46 samples of tomato and peppers treated at 1x; one sample bore pyriproxyfen residues at 0.105 ppm. The available data *do not* support the proposed tolerance of 0.1 ppm for residues of pyriproxyfen in/on fruiting vegetables. The appropriate tolerance level for pyriproxyfen in/on fruiting vegetables is 0.2 ppm. A revised Section B reflecting this change is needed.

7b. **Citrus Fruit**: The submitted field trial data on citrus fruits are adequate. Geographic representation of tests on grapefruit, lemons, and oranges conformed to OPPTS Series 860 guidelines and an adequate number of samples was analyzed. Residues of pyriproxyfen were <0.01-0.24 ppm in/on 52 samples of oranges, lemons, and grapefruits treated at 1x. The available data support the proposed tolerance of 0.3 ppm for residues of pyriproxyfen in/on citrus fruit.

7c. **Tree Nuts**: The submitted field trial data on almonds are adequate. Residues of pyriproxyfen were non-detectable (<0.01 ppm) in/on 12 samples of nutmeat and 0.26-1.40 ppm in/on 12 samples of hulls harvested 16-21 days following the last of three foliar applications of pyriproxyfen (0.86 lb/gal) at ~0.11 lb ai/A/application (~0.33 lb ai/A/season; 1x the proposed seasonal rate). Residues of pyriproxyfen were <0.02 ppm (<LOQ) and 0.96-3.32 ppm in/on four samples each of nutmeat and hulls treated at 2x the proposed rate.

7d. The available data support the proposed tolerance of 2.0 ppm for residues of pyriproxyfen in/on almond hulls.

7e. The submitted data are inadequate to support the proposed tolerance for residues in/on tree nuts because residue data on the representative commodity pecans were not provided. The petitioner has provided data from a total of 10 field trials, 6 on almonds submitted with this petition, and 4 field trials on walnuts that were previously reviewed, all performed in Region 10. Additional data from 5 trials depicting residues of pyriproxyfen in/on pecans conducted in the Regions specified in OPPTS GLN 860.1500 are required. The trials on pecans should include at least one side-by-side trial using spray oil as an adjuvant. Alternatively, the petitioner may propose a tolerance for residues in/on almonds. The data for almonds and walnuts indicates that residues of pyriproxyfen were <0.02 ppm (<LOQ) in/on 20 samples of nutmeat ~21 days following the last of three foliar applications totaling 0.33 lb ai/A (1x the proposed rate).

OPPTS GLN: 860.1520: Processed Food/Feed

8a. **Oranges**: The submitted orange processing study is adequate and indicates that residues of pyriproxyfen do not concentrate in juice, but concentrate by 74.6x in citrus

oil and 6.4x in dried pulp. Based upon these concentration factors and the highest average field trial (HAFT) residues in/on oranges of 0.22 ppm, the proposed tolerances for pyriproxyfen residues in citrus oil and in dried pulp were 20.0 and 1.5 ppm, respectively. The citrus oil tolerance is appropriate; however, FIFRA §6(a)2 data from California suggests that a dried pulp tolerance of 2.0 ppm is needed (D253882, W. Donovan, 22-MAR-1999). Therefore, a revised Section F should be submitted specifying a 2.0 ppm tolerance for citrus pulp, dried.

8b. The submitted processing study indicates that residues of 4'-OH-PYR in orange fractions processed from whole oranges bearing weathered residues of 4'-OH-PYR (0.02 ppm) do not concentrate in juice, but concentrate in oil (60.0x) and dried pulp (5.5x). No tolerances are required for residues of 4'-OH-PYR in citrus commodities as pyriproxyfen *per se* is the residue of concern.

8c. **Tomatoes**: The submitted tomato processing study is adequate. Pyriproxyfen residues were 0.04 ppm in whole tomatoes, 0.02 ppm in paste, and <0.01 ppm in puree. As there was no concentration, separate tolerances for tomato paste and puree are not required.

OPPTS GLN: 860.1480: Meat/Milk/Poultry/Eggs

9. Based on adequate ruminant and poultry metabolism studies, and an adequate cattle feeding study, HED previously concluded that secondary residues in animal commodities are not likely from pyriproxyfen uses (D238190, W. Donovan, 07-DEC-1998). The proposed new uses in the present petition do not significantly change the maximum theoretical dietary burden for cattle. Therefore, tolerances for residues of pyriproxyfen in animal commodities are not required at this time.

OPPTS GLNs 860.1850 and 860.1900: Confined/Field Accumulation in Rotational Crops

10. An adequate confined rotational crop study was conducted in support of the cotton petition (PP#6F4737, DP Barcodes D228556, D228925, and D228926, J. Garbus, 06-MAY-1997). HED concludes that a 30-day plantback interval restriction for rotational crops should be added to the pyriproxyfen label for fruiting vegetables. A revised Section B is needed.

Other Considerations

11. There are no CODEX, Canadian, or Mexican tolerances for pyriproxyfen residues in/on citrus, fruiting vegetables, or tree nuts; thus, international harmonization is not an issue at this time. Pyriproxyfen is scheduled as a new compound for JMPR review (both toxicology and residue chemistry) in 1999.

12. Adequate product chemistry data for the 97% SUMILARV technical product (EPA Reg. No. 10308-11) have been submitted in conjunction with PP#6F04737 (DP Barcode D228556, J. Garbus, 06-MAY-1997). The manufacturing impurities are not expected to pose residue problems at the maximum proposed use rate.

RECOMMENDATIONS

Provided Sections B and F are revised as specified in Conclusions 1, 7a, 7e, 8a, and 10, RAB1 concludes there are no residue chemistry data requirements that would preclude the establishment of permanent tolerances for pyriproxyfen in/on citrus, fruiting vegetables, and almonds. Until satisfactory pecan crop field trial data are submitted, RAB1 cannot recommend in favor of permanent tolerances for pyriproxyfen in/on tree nuts. A human-health risk assessment will be prepared as a separate document.

DETAILED CONSIDERATIONS

OPPTS 830 Series GLNs: Product Properties

Adequate product chemistry data for the 97% SUMILARV technical product (EPA Reg. No. 10308-11) have been submitted in conjunction with PP#6F04737 (DP Barcode D228556, J. Garbus, 06-MAY-1997). The manufacturing impurities are not expected to pose residue problems at the maximum proposed use rate.

OPPTS GLN 860.1200: Proposed Uses

The petitioner provided specimen labels for a 0.86 lb/gal emulsifiable concentrate (EC) formulation (product name: KNACK™ Insect Growth Regulator) and a 2.9 lb/gal EC (product name: ESTEEM™ Insect Growth Regulator) including proposed uses on almond, citrus, tomato, pepper, and walnuts. The proposed use patterns are described below.

Tree Nuts (almonds and walnuts): Both ECs are proposed for multiple foliar applications to almonds and walnuts at 40-50 g ai/A/application (0.09-0.11 lb ai/A/application) for early and late season insect control. The labels specify a maximum use rate of 150 g ai/A/season (0.33 lb ai/A/season), implying a maximum number of three applications allowed each season. The proposed labels specify a 21-day preharvest interval (PHI); however, a minimum RTI is not indicated. Applications are to be made in 100-400 gals/A; however, the type of application equipment (ground or aerial) is not specified on the labels. The use directions for walnuts allow the addition of oil at 1-2% to the spray mixture. The labels for almonds also allow the application of pyriproxyfen with spray oil at delayed dormant using manufacturer specified rates (quantity unspecified).

Citrus Fruits: Both ECs are proposed for multiple foliar applications to citrus fruits at up to 50 g ai/A/application (0.11 lb ai/A/application). The label allows a maximum of three applications per year, and specifies a maximum use rate of 150 g ai/A/season (0.33 lb ai/A/season). The proposed labels specify a 1-day PHI, but do not indicate a minimum RTI. Applications are to be made in 200-1500 gal of water/A, and oils may be added to the spray volume according to manufacturer specified rates (quantity unspecified). The labels do not specify the type of application equipment allowed.

Fruiting Vegetables (peppers and tomatoes): Both ECs are proposed for multiple foliar applications to peppers and tomatoes at 20-30 g ai/A/application (0.04-0.07 lb ai/A/application). The label allows a maximum of three applications per year, and specifies a maximum use rate of 80 g ai/A/season (0.18 lb ai/A/season). The proposed labels specify a 14-day PHI, but do not indicate a minimum RTI. Applications are to be made using ground equipment in 10-150 gal of water/A.

The proposed EC labels specify a restricted entry interval of 12 hours. In addition, the labels specify that applications are not to be made directly to water, to areas where surface water is present, to intertidal areas below the mean high water mark, or through any type of irrigation system.

Conclusions: The proposed use directions for the 0.86 and 2.9 lb ai/gal ECs are inadequate. The labels should be amended to specify a minimum RTI for each of the crops. The proposed labels for almonds, citrus, and walnuts should be amended to specify the type of application equipment (ground or aerial equipment) allowed. In addition, for almonds and citrus, the labels should specify the quantity of spray oil that may be added to the final spray volume. A revised Section B should be submitted.

OPPTS GLN 860.1300: Nature of the Residue - Plants

Tomatoes

Valent submitted data from a study (citation listed below) investigating the metabolism of [^{14}C]pyriproxyfen in tomatoes. The in-life and analytical phases of the study were conducted by Ricerca, Inc., Environmental and Metabolic Fate (Painesville, OH).

> MRID 44638301 Panthani, A.; D. Difrancesco (1997) A Plant Metabolism Study with ^{14}C-S-71639 (Pyriproxyfen) in Tomato Plants: Lab Project Number: 95-0015: 6318-95-0015-EF-001: REPORT/S-71639. Unpublished study prepared by Ricerca, Inc. 191 p. {OPPTS 860.1300}.

The petitioner conducted studies with [^{14}C]pyriproxyfen separately labeled in the pyridyl ring (labeled at the 2- and 6- positions) and the phenoxyphenyl ring (uniformly labeled). The

pyridyl- and phenyl-labeled test substances were diluted with unlabeled emulsifiable concentrate formulation blank in water to form aqueous suspensions with specific activities of 98,436 dpm/μg and 100,537 dpm/μg (radiochemical purities of 98.2-100% and 97.9-100%). Nominal application rates were 60 or 240 g ai/A/application (2 and 8x the maximum proposed rate for fruiting vegetables). Three applications of each formulated test substance were made at each rate to three tomato plants 35, 21, and 7 days before harvest.

Tomato fruits, immature and mature, and vines were collected 7 days after the last treatment. Samples were stored at -20°C until analysis. Eight tomatoes were collected from each treatment group for processing, initiated on the day of harvest at Ricerca. Initially tomatoes were washed with acetonitrile, and the surface washes pooled by treatment group. The washed fruits were homogenized and centrifuged to separate the juice from the pomace. The juice was decanted and the pomace ground with dry ice. Juice and pomace samples were stored at -20°C until analysis.

Total radioactive residues (TRR)

Subsamples of tomato pomace were homogenized with dry ice and total radioactive residues were determined by liquid scintillation counting (LSC) following combustion. TRR in subsamples of the surface wash and juice were determined by direct LSC. The TRR are presented in Table 1. The detection limits (LODs) for the radioassay were 0.0001 ppm for both labels. The petitioner calculated TRR in whole tomato fruit by summing the radioactivity in the surface wash, juice, and pomace fractions. In addition, TRR was determined using values obtained from a pomace solvent extract and remaining pomace tissue summed with rinse and juice residues. These latter values were used to calculate percent TRR in isolated fractions and components.

Table 1. Total radioactive residues (TRR) in samples from tomatoes treated with [^{14}C]pyriproxyfen at 180 g ai/A (0.396 lb ai/A; ~2x the maximum seasonal rate) or 720 g ai/A (~8x the maximum seasonal rate).

Fraction	TRR, ppm [^{14}C]pyriproxyfen equivalents	
	Pyridyl Label	Phenyl Label
180 g ai/application (2x)		
Surface wash	0.005	0.011
Pomace [a]	0.175	0.292
Juice	0.085	0.048
Whole fruit [b]	0.265 (0.259)	0.351 (0.335)
720 g ai/application (8x)		
Surface wash	0.056	0.104
Pomace [c]	1.000	0.756
Juice	0.389	0.130
Whole fruit [c]	1.446	0.990

[a] Radioactivity in pomace is the sum of residues in acetonitrile/1% acetic acid pomace extract and extracted pomace tissue.

[b] TRR for whole tomato was calculated by summing the radioactivity of surface wash, pomace, and juice. TRR values in parentheses include radioactivity in combusted unextracted pomace tissue.

[c] Represents radioactivity detected following combustion of unextracted pomace.

Extraction and hydrolysis of residues

Residues in tomato pomace were extracted with acetonitrile:1% acetic acid (90:10). Juice and surface washes were concentrated prior to further analysis. Solubilized fractions were submitted to HPLC analysis to obtain initial residue profiles. Polar HPLC fractions and those with unresolved components were subjected to hydrolysis with 6.0 N HCl for 2 hours at 70-80°C. In addition, the fraction containing the 2-OH-PY metabolite conjugate was hydrolyzed in 1.0 N NaOH at 40°C overnight. Hydrolyzed samples were analyzed by HPLC. The distribution of ^{14}C-activity in individual extracts of tomato juice, surface wash, and pomace from the 2x treatment is presented in Table 2.

Characterization/identification of residues

Tomato juice, surface washes, and pomace extracts were analyzed by HPLC using a Maxsil C_{18} column and three mobile phase gradients of acidified water (1% acetic acid):ACN. Nonlabeled standards were detected by UV (254 nm), and radioactivity was quantitated by fraction collection and radioactive flow detection (LSC). Isolated fractions and metabolites were analyzed by TLC using the solvent system toluene:ethyl acetate:acetic acid (7:3:0.1, v/v/v). Radioactivity was measured with a Bioscan Imaging Scanner System 200, and

nonlabeled standards were observed under UV light. Metabolites were identified by cochromatography with the following reference standards: pyriproxyfen; 4-(4-hydroxyphenoxy)phenyl (RS)-2-(2-pyridyloxy)propyl ether **(4'-OH-PYR)**; 4-hydroxyphenyl (RS)-2-(2-pyridyloxy)propyl ether **(DPH-PYR)**; (RS)-2-hydroxypropyl 4-phenoxyphenyl ether **(POPA)**; 4-(4-hydroxyphenoxy) phenyl (RS)-2-hydroxypropyl ether **(4'-OH-POPA)**; 4-phenoxyphenol **(POP)**; 4,4'-oxydiphenol **(4'-OH-POP)**; (RS)-2-(2-pyridyloxy)propyl alcohol **(PYPA)**; (RS)-2-(2-pyridyloxy)propionic acid **(PYPAC)**; and 2-hydroxypyridine **(2-OH-PY)** (see Attachment 2 for structures of identified metabolites).

In order to confirm identities of certain metabolites, components were isolated and purified from the exaggerated rate samples and analyzed by GC/MS. The 2-OH-PY peak from pyridyl-labeled juice was converted to the p-bromophenacyl derivative and compared to the derivative standard using HPLC, TLC, and GC/MS. Residue components identified and characterized are summarized in Table 3.

Storage stability

The dates of all analyses and study completion were not specifically stated. However, HPLC profiles of residues in pomace extract and juice were obtained 8 days after harvest and 4.5 months later. The initial and final HPLC profiles were presented side-by side and were very similar. The dates on the chromatograms provided indicate that the final profile was obtained after analyses were completed.

Conclusions: The tomato metabolism study is adequate. Total radioactive residues in whole fruit, calculated by summing residues in surface wash, juice, and pomace were 0.265 ppm in tomatoes treated with pyridyl labeled [^{14}C]pyriproxyfen and 0.351 ppm in tomatoes treated with phenyl labeled [^{14}C]pyriproxyfen at 2x the maximum seasonal rate and harvested 7 days following the last of three applications. ^{14}C-Residues in juice accounted for 13-32% of the whole fruit TRR, pomace contained 66-83%, and surface washes accounted for 2-3%. Nonextractable residues accounted for only ~5% TRR.

The parent pyriproxyfen was the major component of the residue, accounting for 50-68% of the TRR. Related metabolites were present in free and conjugated forms. PYPA (sum of free and bound forms) comprised 10.9% of the residue in the pyridyl labeled tomatoes. 4'-OH-PYR and DPH-PYR were formed from both labeled compounds at 5-6% and 2% TRR, respectively. In phenyl-labeled tomatoes 4'-OH-POPA and 4'-OH-POP (free and bound) accounted for 2.5 and 2% TRR and in pyridyl-labeled tomatoes PYPAC (free and bound) and 2-OH-PY (as the conjugate) respectively accounted for 7.9 and 4.9%. The identities of parent and metabolites were determined by HPLC and confirmed by TLC and GC/MS.

Based on this study, metabolism of pyriproxyfen in tomatoes proceeds by hydroxylation and cleavage of the phenoxy ether linkage. Primary metabolites formed are further metabolized to

more polar products by oxidation or conjugation reactions. Similar metabolic pathways were observed for the metabolism of pyriproxyfen in apples, cotton, goats, and hens.

Accordingly, the MARC decided on 10-NOV-1998 that the residue of concern in plants is pyriproxyfen *per se* (DP Barcode D250953, W. Donovan & W. Dykstra, 19-NOV-1998), unless a significantly different metabolic pathway is identified for a given crop. This finding confirms the 15-JUL-1996 MARC decision rendered for cotton (DP Barcode D228395, R. Loranger, 10-SEP-1996).

Table 2. Distribution and characterization/identification of radioactive residues in/on tomatoes treated with [^{14}C]pyriproxyfen at 180 grams ai/A (0.396 lb ai/A; 2x the proposed maximum seasonal rate).

Fraction	% TRR	ppm	Characterization/Identification [a]		
Phenyl Label					
Whole Tomato Fruit (TRR = 0.351 ppm)					
ACN surface wash	3.1	0.011	HPLC analysis resolved:		
			Pyriproxyfen	2.6% TRR	0.009 ppm
			4'-OH-PYR (free)	0.1% TRR	<0.001 ppm
			Diffuse	0.4% TRR	<0.002 ppm
Juice	13.7	0.048	HPLC analysis resolved:		
			4'-OH-POPA(conj)	1.4% TRR	0.005 ppm
			4'-OH-POP (conj)	1.4% TRR	0.005 ppm
			DPH-PYR (conj)	1.1% TRR	0.004 ppm
			Unknowns/unresolved (each @<2% TRR, 0.007 ppm)		
				9.3% TRR	0.033 ppm
			Diffuse	0.3% TRR	0.001 ppm
Pomace	83.2	0.292 [b]	Extracted with ACN:1% HOAc		
Extracted	78.6	0.276	HPLC analysis resolved:		
			Pyriproxyfen	65.0% TRR	0.228 ppm
			4'-OH-PYR (free)	5.7% TRR	0.020 ppm
			4'-OH-POPA (conj)	1.1% TRR	0.004 ppm
			4'-OH-POP (conj)	0.6% TRR	0.002 ppm
			DPH-PYR (conj)	1.1% TRR	0.004 ppm
			Unknowns	3.4% TRR	0.012 ppm
			Diffuse	1.7% TRR	0.006 ppm
Nonextractable	4.6	0.016	Not further analyzed		
Pyridyl Label					
Whole Tomato Fruit (TRR = 0.265 ppm)					
ACN Surface wash	1.9	0.005	HPLC analysis resolved:		
			Pyriproxyfen	1.5% TRR	0.004 ppm
			4'-OH-PYR (free)	0.1% TRR	<0.001 ppm
			Diffuse	0.4% TRR	0.001 ppm
Juice	32.1	0.085	HPLC analysis resolved:		
			PYPAC (free)	3.8% TRR	0.010 ppm
			PYPAC (conj)	3.0% TRR	0.008 ppm
			PYPA (free)	2.6% TRR	0.007 ppm
			PYPA (conj)	6.8% TRR	0.018 ppm
			2-OH-PY (conj)	4.9% TRR	0.013 ppm
			DPH-PYR (conj)	1.1% TRR	0.003 ppm
			Unknowns/unresolved (each @ <1.5% TRR, 0.004 ppm)		
				8.2% TRR	0.022 ppm
			Diffuse	0.4% TRR	0.004 ppm
Pomace	66.0	0.175 [b]	Extracted with ACN:1% HOAc		
Extracted	60.8	0.161	HPLC analysis resolved:		
			Pyriproxyfen	48.3% TRR	0.128 ppm
			4'-OH-PYR (free)	4.5% TRR	0.012 ppm
			PYPAC (free)	1.1% TRR	0.003 ppm
			PYPA (free)	1.5% TRR	0.004 ppm
			DPH-PYR (conj)	0.8% TRR	0.002 ppm
			Unknowns	2.6% TRR	0.007 ppm
			Diffuse	1.9% TRR	0.005 ppm
Nonextractable	5.3	0.014	Not further analyzed		

(continued; footnotes follow)

[a] Conjugated metabolites were identified as the free metabolite following acid hydrolysis.
[b] TRR in pomace is the sum of residues in acetonitrile/1% acetic acid pomace extract and extracted pomace tissue.

Table 3. Summary of radioactive residues characterized/identified in tomatoes treated with [^{14}C]pyriproxyfen at 180 grams ai/A (0.396 lb ai/A; 2x the proposed maximum seasonal rate).

	Phenyl Label (TRR = 0.351 ppm)		Pyridyl Label (TRR = 0.265 ppm)	
Fraction	% TRR	ppm	% TRR	ppm
Identified [a]				
Pyriproxyfen	67.6	0.237	49.8	0.132
4'-OH-PYR (free)	5.8	0.020	4.6	0.012
4'-OH-POPA (conj)	2.5	0.009	--	--
4'-OH-POP (conj)	2.0	0.007	--	--
2-OH-PY (conj)	--	--	4.9	0.013
DPH-PYR (conj)	2.2	0.008	1.9	0.005
PYPA (free)	--	--	4.1	0.011
PYPA (conj)	--	--	6.8	0.018
PYPAC (free)	--	--	4.9	0.013
PYPAC (conj)	--	--	3.0	0.008
Total identified	**80.1**	**0.281**	**80.0**	**0.212**
Characterized				
Unknowns/unresolved	12.7	0.045	10.9	0.029
Diffuse	2.4	0.009	3.8	0.010
Total identified/characterized	**95.2**	**0.335**	**94.7**	**0.251**
Nonextractable	4.6	0.016	5.3	0.014

[a] See Attachment 2 for the full chemical name and chemical structure of the identified metabolites.

OPPTS GLN 860.1300: Nature of the Residue - Animals

No animal metabolism data were submitted with this petition. Ruminant and poultry metabolism studies have previously been submitted and reviewed (PP#6F04737, DP Barcode D228556, J. Garbus, 06-MAY-1997) in conjunction with a petition for cotton. The animal metabolism studies demonstrated that the transfer of ^{14}C-residues to tissues was low. Radioactivity in goat milk, muscle, and tissues accounted for less than 2% of the administered dose. Radioactivity in poultry eggs, muscle, and tissue accounted for ~2.7% of the administered dose.

OPPTS GLN 860.1340: Residue Analytical Methods-Plants

In conjunction with the residue studies on citrus fruit (MRIDs 44630104-06), the petitioner submitted a method description and concurrent recovery data for a GC/NPD and HPLC method (RM-33P-1-3) used to determine residues of pyriproxyfen and its metabolite 4'-OH-PYR in citrus fruit. The method has been adequately radiovalidated, has undergone a successful ILV (D238190, W. Donovan, 07-DEC-1998), and has also been recommended for Agency method validation on apples and oranges (D252371, W. Donovan, 28-JAN-1999). The petitioner indicated that the GC/NPD method RM-33P-1-1, a precursor to method RM-33P-1-3 that does not include the analysis of 4'-OH-PYR by HPLC, was used to determine residues of pyriproxyfen in/on orange commodities. Also, for samples from two orange trials (Porterville, CA-2, and Richgrove, CA) residues of 4'-OH-PYR were determined using HPLC/UV method RM-33M-2. This method is based on method RM-33M-1 that was previously deemed adequate for data collection on pome fruit and described in detail in the review of the petition for permanent tolerances on pome fruit (DP Barcode D238190, W. Donovan, 07-DEC-1998). A brief description of the methods follow:

Method RM-33P-1-3: Residues of pyriproxyfen and 4'-OH-PYR in/on citrus fruits are extracted with acetone, filtered, and concentrated. The residues are sequentially partitioned into ACN:hexane and DCM:0.5% NaCl solution, and cleaned-up using silica gel chromatography. Pyriproxyfen residues are then analyzed by GC/NPD, and residues of 4'-OH-PYR are analyzed by HPLC with fluorescence detection. The LOQ for both analytes is 0.02 ppm; the LOD is 0.01 ppm for each analyte.

In conjunction with the residue studies on fruiting vegetables (MRID 446301-03 and -07), the petitioner submitted method descriptions and validation data for GC/NPD methods RM-33P-8 and -9 used to determine residues of pyriproxyfen and PYPA in/on tomato and peppers. Method RM-33P-8 was slightly modified with respect to elution volume of PYPA from the SPE clean-up to improve on recoveries from peppers, and the revised version was designated method RM-33P-9.

Method RM-33P-9: In brief, residues of pyriproxyfen and PYPA in/on tomato and peppers are extracted with ACN or ACN:H_2O (4:1, v/v), concentrated to remove ACN, and PYPA conjugates in the extracts are hydrolyzed using 1N HCl (reflux, 2 hrs). Residues of pyriproxyfen are partitioned into DCM (the aqueous phase is retained for analysis of PYPA), dried over sodium sulfate, and concentrated to dryness. Pyriproxyfen residues are redissolved in toluene, cleaned-up on a silica gel column, and analyzed by GC/NPD. Residues of PYPA in the aqueous phase are neutralized using a 10% NaOH solution, partitioned into DCM, dried over sodium sulfate, and concentrated to dryness. The residues are then taken up in hexane:EtOAc, cleaned-up by SPE chromatography, and analyzed by GC/NPD. The LOQ for both analytes is 0.02 ppm; the LOD is 0.01 ppm for each analyte.

In conjunction with the almond residue data (MRID 44630102), the petitioner submitted method descriptions and validation data for two GC/NPD and HPLC/FLD methods used to determine residues of pyriproxyfen and 4'-OH-PYR in/on almond nutmeat (method RM-33N-2) and hulls (method RM-33H). Method RM-33N-2 was previously deemed adequate for data collection on walnut nutmeat, and has been recommended for an Agency method validation on walnuts (D252371, W. Donovan, 28-JAN-1999). The method is similar to method RM-33P-1-3, described above. Another similar method, used to determine pyriproxyfen residues in/on cottonseed (RM-33P-2), was previously successfully validated by the Agency in conjunction with a permanent tolerance petition for use on cotton (PP#6F04737, DP Barcode D228556, J. Garbus, 06-MAY-1997).

Method RM-33N-2: Briefly, residues of pyriproxyfen and 4'-OH-PYR are extracted from almond nutmeat with acetone, sequentially partitioned with DCM:0.5% NaCl solution and ACN:hexane, and purified and separated by silica gel chromatography. Residues of pyriproxyfen and 4'-OH-PYR are then determined separately by GC/NPD and HPLC/FLD, respectively. The LOD for pyriproxyfen and 4'-OH-PYR in/on almond nutmeat is 0.01 ppm for each analyte. The validated LOQ for both analytes is 0.02 ppm.

Method RM-33H: In brief, residues of pyriproxyfen and 4'-OH-PYR in/on almond hulls are extracted with MeOH:H_2O (4:1, v/v), and filtered. Residues of pyriproxyfen are partitioned into hexane, and following evaporation of the methanol from the aqueous phase, residues of 4'-OH-PYR are extracted into hexane. The separate extracts are then cleaned-up by silica gel chromatography prior to analysis for pyriproxyfen and 4'-OH-PYR using GC/NPD and HPLC, respectively. The LOQ for both analytes is 0.02 ppm; the LOD is 0.01 ppm for each analyte.

Method recovery data are presented in Tables 4-6. For method validation, control samples of selected crop matrices were fortified with pyriproxyfen and either 4'-OH-PYR or PYPA each at 0.02-5.0 ppm, and were analyzed using the GC and HPLC methods described above. Overall method recoveries of pyriproxyfen were 77-106% in method validation studies (n=28), and 66-121% for concurrent recoveries (n=157). Overall method recoveries of 4'-OH-PYR were 70-112%. Overall recoveries of PYPA were 54-141%, and with the exception of some isolated poor recoveries, were generally acceptable.

Table 4. Method recoveries of pyriproxyfen from fortified samples of crop matrices using GC/NPD and HPLC/FLD methods.

MRID	Commodity	Fortification Level (ppm)	# of Samples	% Recovery of Pyriproxyfen [a]	
				Range	Mean (C.V.)
Method Validation Recoveries					
44630107	Tomato	0.02, 0.1	18	77-106	92 (9.6)
44630105	Oranges	0.02	4	83-96	88 (6.7)
		0.1	6	91-97	94 (2.4)
Concurrent Method Recoveries					
44630102	Almond nutmeat	0.02	6	79-114	93 (12.6)
		0.10	6	80-96	87 (8.8)
	Almond Hulls	0.02	6	74-98	90 (10.2)
		0.01	11	73-105	91 (11.1)
44630104	Grapefruit	0.02, 0.1	12	87-121 (2)	104 (12.0)
44630105	Oranges	0.02, 0.1	27	66-111 (3)	91 (12.6)
	Oranges, whole	0.02, 0.1	2	99, 105	97 (11.8)
	Pulp, dried	0.05, 0.25	2	100, 97	
	Oil	1.0, 5.0	2	115, 111	
	Peel, fresh	0.02, 0.1	2	81, 98	
	juice	0.02, 0.1	2	97, 98	
	Centers	0.02, 0.1	2	79, 81	
44630106	Lemons	0.02, 0.1	10	85-100	92 (7.7)
44630107	Peppers	0.02	16	75-110	94 (9.5)
		0.1	16	81-108	94 (8.8)
44630103	Tomato	0.02	17	68-102 (1)	88 (10.8)
		0.1	16	73-102	89 (8.47)
	Puree	0.02	1	85	86 (1.6)
	Paste	0.02	1	87	

[a] Values in parentheses represent the number of recoveries outside the acceptable range (70-120%).

Table 5. Method recoveries of 4'-OH-PYR from fortified samples of crop matrices using GC/NPD and HPLC methods.

MRID	Commodity	Fortification Level (ppm)	# of Samples	% Recovery of 4'-OH-PYR	
				Range	Mean (C.V.)
Method Validation Recoveries					
44630107	Tomato	0.02, 0.1	18	77-106	92 (9.6)
44630105	Oranges	0.1	6	82-92 [a]	86 (4.0)
		0.5	3	75-83 [a]	78 (5.2)
		0.02	6	88-98	96 (3.9)
		0.1	6	88-98	96 (3.9)
Concurrent Method Recoveries					
44630102	Almond, nutmeat	0.02, 0.1	2	98, 110	104 (8.2)
	Almond, hulls	0.02	6	70-103	82 (16.4)
		0.01	11	82-105	93 (7.3)
44630104	Grapefruit	0.02, 0.1	14	91-112	101 (6.9)
44630105	Oranges	0.02-0.5	16	73-103	88 (11.0)
	Oranges, whole	0.02, 0.1	2	86, 115	97 (10.0)
	Pulp, dried	0.05, 0.25	2	92, 105	
	Oil	1.0, 5.0	2	91, 108	
	juice	0.02, 0.1	2	98, 99	
	Peel, fresh	0.02, 0.1	2	108, 85	
	Centers	0.02, 0.1	2	89, 93	
44630106	Lemons	0.02, 0.1	10	77-94	88 (5.6)

[a] Analyzed using method RM-33M-2. Samples were fortified with 4'-Glu-Pyr and residues of free 4'-OH-PYR analyzed after hydrolysis. As metabolism data indicated 4'-OH-PYR is not conjugated in fruit, the hydrolysis step was removed from method RM-33P-1-3, which was used to analyze most of the orange field trial samples.

Table 6. Method validation recoveries of PYPA from fortified samples of crop matrices using GC/NPD methods.

MRID	Commodity	Fortification Level (ppm)	# of Samples	% Recovery of PYPA	
				Range [a]	Mean (C.V.)
Method Validation Recoveries					
44630107	Tomato	0.02, 0.1	18	84-108	91 (6.3)
Concurrent Method Recoveries					
44630107	Peppers	0.02	15	69-141 (2)	102 (18.0)
		0.1	15	64-140 (2)	96 (20.7)
44630103	Tomato	0.02	17	54-117 (1)	92 (15.4)
		0.1	16	71-118	87 (15.1)
	Puree	0.02	1	90	91 (1.6)
	Paste	0.02	1	92	

[a] Values in parentheses represent the number of recoveries outside the acceptable range (70-120%).

Conclusions: The GC/NPD and HPLC method RM-33P-1-3 is adequate for collecting data on residues of pyriproxyfen and 4'-OH-PYR in/on citrus fruits. Adequate method validation data have been submitted for this method. The method has been adequately radiovalidated using samples from the apple metabolism study, and it has undergone a successful ILV. The method has also been recommended for an Agency method validation (D252371, W. Donovan, 28-JAN-1999). The LOQ is 0.02 ppm for residues of pyriproxyfen and 4'-OH-PYR in/on citrus fruits.

GC/NPD method RM-33P-9 is adequate for collecting data on residues of pyriproxyfen and PYPA in/on tomato and peppers. Adequate method validation data have been submitted for this method, which has been recommended for Agency method validation (D252371, W. Donovan, 28-JAN-1999). The method is similar to method RM-33P-1-3 discussed above. The LOQ is 0.02 ppm for residues of pyriproxyfen and PYPA in/on tomato and peppers.

The GC/NPD and HPLC/FLD method RM-33N-2 is adequate for collecting data on residues of pyriproxyfen and 4'-OH-PYR in/on almond nutmeat. Adequate method validation data have been submitted for this method, which has been recommended for Agency method validation (D252371, W. Donovan, 28-JAN-1999). The LOQ is 0.02 ppm for residues of pyriproxyfen and 4'-OH-PYR in/on almond nutmeat.

The GC/NPD and HPLC/FLD method RM-33H is adequate for collecting data on residues of pyriproxyfen and 4'-OH-PYR in/on almond hulls. Adequate method validation data have been submitted for this method, which has been recommended for Agency method validation (D252371, W. Donovan, 28-JAN-1999). The method is fundamentally similar to RM-33N-2,

discussed above. The LOQ is 0.02 ppm for residues of pyriproxyfen and 4'-OH-PYR in/on almond hulls.

As the HED MARC has concluded that pyriproxyfen *per se* is the residue of concern in plant commodities, the proposed enforcement methods should be amended to remove procedures for the analysis of metabolites of pyriproxyfen (i.e., 4'-OH-PYR and PYPA).

OPPTS GLN 860.1340: Residue Analytical Methods - Livestock Commodities

As tolerances for residues of pyriproxyfen in animal commodities are not required at this time, enforcement methodology for determining residues in livestock are not required.

OPPTS GLN 860.1360: Multiresidue Method

Multiresidue Testing data have previously been provided (PP#6F04737, DP Barcode D228556, J. Garbus, 06-MAY-1997) for pyriproxyfen and its metabolite PYPAC. Pyriproxyfen was recovered from fortified apple and cotton samples through protocols A, C, D, E, and F. The metabolite PYPAC was tested with protocols A, B, C, and D. The results have been forwarded to FDA.

OPPTS GLN 860.1380: Storage Stability Data - Plants

In conjunction with the residue studies on almonds, citrus, and fruiting vegetables (MRIDs 446301-02 through -07), the petitioner conducted studies depicting the stability of residues of pyriproxyfen and its metabolites in crop matrices stored at -20°C. Control samples of almond hulls, oranges, peppers, and tomatoes were fortified with pyriproxyfen and either 4'-OH-PYR or PYPA each at 0.10 ppm and analyzed periodically at frozen storage intervals up to a maximum of 91-280 days. An additional short-term (1 month) study with weekly sampling intervals was conducted on tomato to verify the results of the long-term study. At each sampling interval, a freshly fortified and two stored fortified samples were analyzed using the GC/NPD and HPLC/FLD methods described above. Apparent residues of each analyte were <0.01 ppm ($<$LOD) in controls with the exception of one orange control sample which bore residues of 4'-OH-PYR at 0.015 ppm. Recoveries were corrected for residues in control samples by the petitioner. The results of the storage stability study are presented in Table 7 and reflect uncorrected recovery values.

The storage stability data are adequate and indicate that residues of pyriproxyfen *per se* are stable frozen (-20°C) in almond hulls and oranges for up to 4 months, and are relatively stable in peppers for up to 3 months. Residues of pyriproxyfen in tomato declined by ~25% within one week, and by 40-60% after 1 month of frozen storage.

Residues of 4'-OH-PYR appeared to decline by ~25% after 1 month of storage in almond hulls, but were relatively stable for up to 4 months of storage at -20°C. Residues of 4'-OH-

PYR were stable in oranges after 3 months of frozen storage at -20°C. Residues of PYPA were stable in tomato and peppers after 3 months of storage, but showed an apparent loss of ~35% in tomato after 9 months at -20°C.

Previously reviewed storage stability data (PP#7F04882, DP Barcode D238190, W. Donovan, 07-DEC-1998) indicates that pyriproxyfen and 4'-OH-PYR are stable in walnut nutmeat at -20°C for up to 3 months.

Conclusions: The submitted storage stability data are adequate and indicate that pyriproxyfen is stable at -20°C for up to 4 months in almond hulls and oranges, and for up to 3 months in peppers. In tomato, pyriproxyfen residues declined by ~25% within one week, and by ~40-60% after 1 month of frozen storage at -20°C; however, with the exception of two trials, tomato residue samples were analyzed within approximately one week of sampling. The maximum frozen storage interval from sampling to analysis for almond, citrus, and pepper was < 1-3 months. These data, together with previously submitted data indicating that residues of pyriproxyfen are stable in frozen walnut nutmeat for 3 months, adequately support the residue data submitted for the permanent tolerance petitions for citrus, fruiting vegetables, and tree nuts.

The submitted storage stability data, together with existing storage stability data on walnuts, indicate that residues of 4'-OH-PYR and PYPA are relatively stable in almonds and oranges, and tomato and peppers, respectively, over the storage intervals and conditions reflected in the residue studies (≤3 months at ~-20°C).

Table 7. Stability of pyriproxyfen and its metabolites in various crop matrices fortified with each analyte at 0.1 ppm and stored at -20 °C for up to ~4 months.

Commodity	Storage Interval (days)	Percent Recovery		
		Fresh Fortification	Stored Sample	Stored Sample Corrected [a]
Pyriproxyfen				
Almonds, hulls	0	96	82, 86	--
	32	84	89, 84	103
	129	81	94, 80	107
Oranges	0	95, 95	--	--
	36	84	100, 103	121
	58	89	91, 79	96
	91	97	81, 83	85
	122	94	78, 98	99
Peppers	0	103	105, 101	103
	30	94	82, 82	87
	63	103	78, 72	73
	66	92	71, 68	76
	91	97	84, 76	82

(Continued; footnotes follow)

Commodity	Storage Interval (days)	Percent Recovery		
		Fresh Fortification	Stored Sample	Stored Sample Corrected [a]
Tomato	Short Term Study			
	0	90	97, 90	--
	7	101	78, 72	74
	14	99	60, 71	66
	21	103	54, 61	56
	28	94	81, 72	81
	33	106	68, 72	66
	Long Term Study			
	0	98	97, 90	95
	30	102	40, 39	39
	60	95	42, 49	48
	108	90	31, 33	36
	280	103	49, 56	51
4'-OH-PYR				
Almonds, hulls	0	89	92, 96	--
	32	95	71, 77	78
	130	95	77, 70	77
Oranges	0	86, 82, 84	--	--
	64	108	99, 107	95
	90	103	89, 89	86
PYPA				
Peppers	0	106	106, 102	105
	30	114	114, 107	97
	60	92	90, 92	99
	91	87	92, 86	102
Tomato	0	96	88, 89	91
	30	82	100, 98	108
	60	112	110, 115	100
	108	94	87, 86	92
	280	95	62, 60	64

[a] Calculated by dividing the average recovery of the two stored samples by the fresh fortification recovery.

OPPTS GLN 860.1500: Crop Field Trials

Fruiting Vegetables Group

Peppers

Valent submitted data from 10 field trials conducted in CA (4), FL (1), MI (1), NM (1), NC (1), and TX (2 field trials, Regions 6 and 8) during 1996 and 1997 depicting residues of pyriproxyfen in/on peppers, including three field trials with non-bell peppers (Anaheim Chile, Jalapeno M, and Big Jim). The bell peppers utilized were the King Arthur, Jupiter, Grande Rio 66, Capistrano and CA Wonder varieties. These data were submitted to support a proposed tolerance for residues in/on the fruiting vegetables crop group.

> MRID 44630107 Pensyl, J. (1998) Magnitude of the Residues of Pyriproxyfen and its Degradates in Peppers: Lab Project Number: V-11461: VP-11461: V-11461-A. Unpublished study prepared by Valent USA Corporation and South Texas AG Research. 800 p. {OPPTS 860.1500}

Pyriproxyfen (0.86 lb/gal EC) was applied three times by broadcast foliar application to peppers at nominal rates of 20, 30, and 30 g ai/A/application, at 14-day RTIs, for a seasonal rate of 80 g ai/A (equivalent to ~0.18 lb ai/A, 1x the proposed rate). In addition, at two trial locations a 2x exaggerated rate (40+60+60 g ai/A) was applied. Applications at the 1x rate were made using ground equipment in ~20 gal/A of water with the exception of one trial (FL) in which ~40 gal/A of water were used.

Samples of 24 peppers were harvested 13-14 days following the last application; in two field trials peppers were harvested at 7, 14, 21, and 28 days posttreatment to determine residue decline. Pepper samples were shipped overnight via freezer truck to the Valent Technical Center, Dublin, CA, where they were stored at -20°C. Analyses of pyriproxyfen and PYPA were conducted within 5-65 days using methods RM-33P-8 and -9. Residues in all control samples were below the 0.01 ppm LOD for both analytes. Adequate concurrent recoveries were obtained for both compounds. The results are presented in Table 8.

Among the 20 pepper samples harvested 14 days following 1x treatment, pyriproxyfen was nondetectable (<0.01 ppm) in/on eight, 0.01-0.06 ppm in/on 11 samples, and 0.105 ppm in/on one sample. At 2x, pyriproxyfen was detected at 0.05-0.17 ppm in/on four samples. In the two decline studies residues decreased ~50% in one study and 25% in the other from 7 days posttreatment to 28 days. PYPA was <0.01 ppm in all treated samples.

Table 8. Residues of pyriproxyfen and PYPA in/on **peppers** harvested following the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at 1x or 2x the proposed rate (nominally 80 g ai or 0.18 lb ai/A total).

Trial Location and Date	Total Appl. Rate (lb ai/A)	PHI	Residues (ppm)	
			Pyriproxyfen	PYPA
CA 1996	0.152	14	<0.01, <0.01	<0.01, <0.01
CA 1997	0.180	13	0.02, <0.01	<0.01, <0.01
CA 1997 [a]	0.181	14	0.03, 0.02	<0.01, <0.01
	0.358	14	0.06, 0.05	<0.01, <0.01
CA 1997	0.177	14	0.03, 0.03	<0.01, <0.01
FL 1997	0.176	7	0.10, 0.11	<0.01, <0.01
		14	0.06, 0.11 [b]	<0.01, <0.01
		21	0.05, 0.06	<0.01, <0.01
		28	0.05, 0.05	<0.01, <0.01
	0.348	14	0.17, 0.17	<0.01, <0.01
MI 1997	0.176	14	<0.01, 0.01	<0.01, <0.01
NM 1997 [a]	0.177	7	0.03, 0.05	<0.01, <0.01
		14	0.04, 0.03	<0.01, <0.01
		21	0.03, 0.03	<0.01, <0.01
		28	0.03, 0.03	<0.01, <0.01
NC 1997	0.177	14	<0.01, <0.01	<0.01, <0.01
TX 1997	0.178	14	<0.01, <0.01	<0.01, <0.01
TX 1997 [a]	0.177	14	0.02, 0.01	<0.01, <0.01

[a] Test conducted on non-bell peppers.
[b] The analytical report listed the residue in this sample as 0.105 ppm.

Tomatoes

Valent submitted data from 13 field trials conducted in AZ (1), CA (7), FL (2), GA (1), MI (1), and NJ (1) during 1996 and 1997 depicting residues of pyriproxyfen in/on tomatoes. Commercially important varieties of tomatoes were used in this study: Rio grande Roma, Neura 512, Champion, Sunny, Better Boy, Solamar, Mt. Spring, Champ, Heinz 8892, and CDX 152. These data were submitted to support a proposed tolerance for residues in/on the fruiting vegetables crop group.

MRID 44630103 Pensyl, J. (1998) Magnitude of the Residues of Pyriproxyfen and its Degradates in Tomatoes: Lab Project Number: V-11460-A. Unpublished study prepared by

Valent USA Corporation and California AG Research. 1091 p. {OPPTS 860.1500 & 860.1520}

Pyriproxyfen (0.86 lb/gal EC) was applied three times by broadcast foliar application to tomatoes at nominal rates of 20, 30, and 30 g ai/A/application, at 14-day RTIs, for a seasonal rate of 80 g ai/A (1x the proposed rate, equivalent to ~0.18 lb ai/A). In addition, at four trial locations a 2x exaggerated rate (40+60+60 g ai/A) was applied and two field trials were conducted in which pyriproxyfen was applied at 5x (100+150+150 g ai/A). Applications at the 1x rate were made using ground equipment in 19-21 gal/A of water with the exception of two trials (FL) in which applications were made in 77-100 gal/A of water.

Samples of 24 tomatoes were harvested 13-14 days following the last application; in two field trials tomatoes were harvested at 7, 14, 21, and 28 days posttreatment to determine residue decline. From the 5x application, 150 lbs of tomatoes were harvested for use in a processing study. Tomato samples were shipped overnight via freezer truck to the Valent Technical Center, Dublin, CA, where they were stored at -20°C. Analyses of pyriproxyfen and PYPA were conducted within 0-21 days using methods RM-33P-8 and -9. Residues in all control samples were below the 0.01 ppm LOD for both analytes. Adequate concurrent recoveries were obtained for both compounds. The results are presented in Table 9.

Among the 26 tomato samples harvested 14 days following treatment at 1x, 16 had no detectable pyriproxyfen residue (<0.01 ppm); residues in the other eight samples were 0.01-0.04 ppm. Eight samples treated at 2x bore pyriproxyfen residues of <0.01-0.11 ppm and four 5x treated samples contained 0.02-0.24 ppm. PYPA was <0.01 ppm in all treated samples with the exception of two 5x samples each containing 0.02 ppm. All samples from the two decline studies had no detectable residues.

Table 9. Residues of pyriproxyfen and PYPA in/on **tomatoes** harvested following the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at 1x, 2x, and 5x the proposed rate (nominally 80 g ai or 0.18 lb ai/A total).

Trial Location and Date	Total Appl. Rate (lb ai/A)	PHI	Residues (ppm)	
			Pyriproxyfen	PYPA
AZ 1997	0.179	14	<0.01, <0.01	<0.01, <0.01
CA 1996	0.178	7	<0.01, <0.01	<0.01, <0.01
		14	<0.01, <0.01	<0.01, <0.01
		21	<0.01, <0.01	<0.01, <0.01
		28	<0.01, <0.01	<0.01, <0.01
	0.346	14	<0.01, <0.01	<0.01, <0.01
CA 1996	0.175	14	<0.01, 0.01	<0.01, <0.01
CA 1997	0.178	13	0.02, 0.02	<0.01, <0.01
CA 1997	0.174	13	0.03, 0.04	<0.01, <0.01
CA 1997	0.174	14	0.03, 0.03	<0.01, <0.01
CA 1997	0.175	14	<0.01, <0.01	<0.01, <0.01
	0.351	14	0.01, 0.01	<0.01, <0.01
	0.889	14	0.02, 0.02	<0.01, <0.01
CA 1997	0.177	14	0.03, 0.04	<0.01, <0.01
	0.352	14	0.11, 0.08	<0.01, <0.01
	0.892	14	0.24, 0.21	0.02, 0.02
FL 1997	0.175	14	<0.01, <0.01	<0.01, <0.01
FL 1997	0.175	7	<0.01, <0.01	<0.01, <0.01
		14	<0.01, <0.01	<0.01, <0.01
		21	<0.01, <0.01	<0.01, <0.01
		28	<0.01, <0.01	<0.01, <0.01
GA 1996	0.181	14	<0.01, <0.01	<0.01, <0.01
MI 1997	0.176	14	<0.01, 0.01	<0.01, <0.01
	0.355	14	0.01, 0.01	<0.01, <0.01
NJ 1997	0.179	14	<0.01, <0.01	<0.01, <0.01

Conclusions: The submitted field trial data on fruiting vegetables are adequate. Geographic representation of field trials on peppers and tomatoes conformed to OPPTS Series 860 guidelines and an adequate number of samples was analyzed. An adequate variety of commercially important peppers and tomatoes were included in the study. Residues of pyriproxyfen were <0.01-0.06 ppm in/on 46 samples of tomato and peppers treated at 1x; one sample bore pyriproxyfen residues at 0.105 ppm. The available data *do not* support the

proposed tolerance of 0.1 ppm for residues of pyriproxyfen in/on fruiting vegetables. The appropriate tolerance level for pyriproxyfen in/on fruiting vegetables is 0.2 ppm. A revised Section F should be submitted reflecting this change.

Citrus Fruits Group

Oranges:

Valent submitted data from 13 field trials conducted in CA (3), FL (9), and TX (1, Region 6) during 1995-1998 depicting residues of pyriproxyfen in/on oranges (citation noted below). The oranges used in this study include Navel, No. 132 Navel, Washington Navel, Lane Navel, Linda Valencia, MidSweet, Everhard Navel, and Rhode Red Valencia. These data were submitted to support a proposed tolerance for residues in/on the citrus fruits crop group.

MRID 44630105 Green, C. (1998) Magnitude of the Residue of Pyriproxyfen in/on Oranges and Orange Processing Fractions: Lab Project Number: V-95-11121: V11121-A: V11121-B. Unpublished study prepared by Valent USA Corporation and South Texas AG Research. 1316 p. {OPPTS 860.1500 & 860.1520}

Pyriproxyfen (0.86 lb/gal EC) was applied three times by broadcast foliar application to oranges at nominal rates of 50 g ai/A lb ai/A/application, at 21-day RTIs, for a seasonal rate of 150 g ai/A (equivalent to ~0.33 lb ai/A, 1x the proposed rate). In four tests, samples were collected at 1, 7, and 21 days posttreatment to determine residue decline. In addition, at two trial locations a 2x exaggerated rate (~100 g ai/A/application) was applied. Applications at the 1x rate were made using airblast sprayers in ~200 gal/A of water with spray oil added at 0.5% v/v.

Samples of 24 mature fruit were harvested from each trial 1 day following the last application; in three tests oranges were harvested at 1, 7, and 21 days posttreatment to determine residue decline. Oranges were frozen following collection and shipped within 2-22 days via freezer truck to the Valent Technical Center, Dublin, CA, where eight oranges were separated into peel and interior flesh and the rest were stored at -20°C. Analyses of pyriproxyfen were conducted within 90 days using methods RM-33P-1-1 and RM-33P-1-3. 4-OH-PYR residues were analyzed using method RM-33M-2 (two CA trials) and RM-33P-1-3. Residues in all control samples were below the 0.01 ppm LOD for both analytes. Adequate concurrent recoveries were obtained for both compounds. The results are presented in Table 10.

Pyriproxyfen residues were 0.05-0.23 ppm in/on 26 orange samples harvested 1 day after the last of three applications at 1x. At 2x, pyriproxyfen was detected at 0.36-0.41 ppm in/on four samples. In the four residue decline studies, residues decreased ~33% in one field trial and remained relatively constant in three others from 1-21 days posttreatment. After 1x treatment, residues of 4'-OH-PYR were non-detectable (<0.05 or <0.01 ppm) in/on 12 samples, and

0.01-0.02 ppm in/on 6 samples. At 2x, pyriproxyfen was detected at 0.01-0.02 ppm in/on four samples.

The results of the separate analysis of two samples of orange peel and interior flesh from oranges treated at 1x or 2x are presented in Table 11. The data indicate that residues of pyriproxyfen and 4'-OH-PYR are found primarily in the peel.

Table 10. Residues of pyriproxyfen and 4'-OH-PYR in/on **oranges** harvested following the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at 1x or 2x (nominally 150 g ai or 0.33 lb ai/A total).

Trial Location and Date	Total Appl. Rate (lb ai/A)	PHI	Residues (ppm)	
			Pyriproxyfen	4'-OH-PYR
CA 1996	0.33	1	0.09, 0.05	<0.05, <0.05 [a]
CA 1996	0.33	1	0.11, 0.15	<0.05, <0.05 [a]
CA 1996	0.33	1	0.14, 0.15	NA [b]
		7	0.10, 0.18	NA
		21	0.14, 0.16	NA
	0.17 [c]	1	0.10, 0.09	NA
		7	0.11, 0.09	NA
		21	0.09, 0.10	NA
FL 1997	0.33	1	0.21, 0.20	0.02, 0.02
FL 1997	0.33	1	0.15, 0.13	<0.01, <0.01
FL 1997	0.33	1	0.12, 0.14	<0.01, <0.01
FL 1997	0.33	1	0.21, 0.22	<0.01, <0.01
FL 1997	0.33	1	0.16, 0.16	0.01, 0.01
FL 1997	0.33	1	0.21, 0.23	<0.01, <0.01
	0.66	1	0.40, 0.36	0.02, 0.01
FL 1995	0.33	1	0.18, 0.13	NA
		7	0.12, 0.13	NA
		21	0.10, 0.11	NA
FL 1995	0.33	1	0.14, 0.15	NA
		7	0.13, 0.19	NA
		21	0.13, 0.13	NA
FL 1997	0.33	1	0.21, 0.23	0.01, 0.01
	0.66	1	0.40, 0.41	0.02, 0.02
TX 1997	0.33	1	0.13, 0.14	<0.01, <0.01

[a] NA = Not Analyzed.

[b] Analyzed using method RM-33M-2 for which the LOD and LOQ for 4'-OH-PYR are 0.05 and 0.1 ppm, respectively. All other samples were analyzed for 4'-OH-PYR using method RM-33P-1-3 for which the LOD and LOQ are 0.01 and 0.02 ppm, respectively.

[c] Application rate represents 0.5x the proposed rate (0.33 lb ai/A total).

Table 11. Residues of pyriproxyfen and 4'-OH-PYR in/on orange peel and flesh harvested 1 day following the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at 1x or 2x (nominally 150 g ai or 0.33 lb ai/A total; 1x).

Trial Location and Date	Commodity	Total Appl. Rate (lb ai/A)	Residues (ppm)	
			Pyriproxyfen	4'-OH-PYR
FL 1998	Orange peel	0.33	0.76, 0.62	0.03, 0.02
		0.66	2.1, 2.1	0.05, 0.06
	Orange flesh	0.33	<0.01, <0.01	<0.01, <0.01
		0.66	0.01, 0.01	<0.01, <0.01

Lemons

The petitioner submitted data from 6 field trials conducted in AZ, CA (4), and FL during 1996-1997 depicting residues of pyriproxyfen in/on lemons (citation noted below). These data were submitted to support a proposed tolerance for residues in/on the citrus fruits crop group.

MRID 44630106 Green, C. (1998) Magnitude of the Residue of Pyriproxyfen in/on Lemons: Lab Project Number: V-96-11457: V-11457: V-11457-A. Unpublished study prepared by Valent USA Corporation and Southeast AG Research. 545 p. {OPPTS 860.1500}

Pyriproxyfen (0.86 lb/gal EC) was applied three times by broadcast foliar application to lemons at nominal rates of 50 g ai/A lb ai/A/application, at 21-day RTIs, for a seasonal rate of 150 g ai/A (equivalent to ~0.33 lb ai/A, 1x the proposed rate). In addition, at two trial locations a 2x exaggerated rate (~100 g ai/A/application) was applied. Applications at the 1x rate were made using airblast sprayers in 193-212 gal/A of water with spray oil added at 0.5% v/v.

Samples of 16 or 24 mature fruit were harvested from each trial 1 day following the last application. Lemons were frozen following collection and shipped within 1-6 days by overnight courier (on dry ice) to the Valent Technical Center, Dublin, CA, where the samples were stored at ~-20°C. Analyses of pyriproxyfen and 4'-OH-PYR were conducted within 91 days using method RM-33P-1-3. Residues in all control samples were below the 0.01 ppm LOD for both analytes. Adequate concurrent recoveries were obtained for both compounds. The results are presented in Table 12.

Pyriproxyfen residues were <0.01-0.24 ppm in/on 12 lemon samples harvested 1 day after the last of three applications at 1x. At 2x, pyriproxyfen was detected at 0.55 and 0.58 ppm in/on two treated samples. 4'-OH-PYR was <0.01 ppm in all treated samples.

Table 12. Residues of pyriproxyfen and 4'-OH-PYR in/on **lemons** harvested following the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at 1x or 2x (nominally 150 g ai or 0.33 lb ai/A total).

Trial Location and Date	Total Appl. Rate (lb ai/A)	PHI	Residues (ppm)	
			Pyriproxyfen	4'-OH-PYR
AZ 1996	0.33	1	<0.01, <0.01	<0.01, <0.01
CA 1996	0.33	1	0.15, 0.10	<0.01, <0.01
CA 1997	0.33	1	0.17, 0.19	<0.01, <0.01
	0.66	1	0.58, 0.55	<0.01, <0.01
CA 1997	0.33	1	0.06, 0.10	<0.01, <0.01
CA 1997	0.33	1	0.24, 0.20	<0.01, <0.01
FL 1997	0.33	1	0.16, 0.15	<0.01, <0.01

Grapefruit

Valent submitted data from 7 field trials conducted in CA (3), FL (3), and TX (1, Region 6) during 1996 and 1997 depicting residues of pyriproxyfen in/on grapefruit (citation noted below). These data were submitted to support a proposed tolerance for residues in/on the citrus fruits crop group.

MRID 44630104 Green, C. (1998) Magnitude of the Residue of Pyriproxyfen in/on Grapefruit: Lab Project Number: V-96-11458: VP-11458: V-11458-A. Unpublished study prepared by Valent U.S.A. Corp. V-11458-A. Unpublished study prepared by Valent USA Corporation and South Texas AG Research. 633 p. {OPPTS 860.1500}

Pyriproxyfen (0.86 lb/gal EC) was applied three times by broadcast foliar application to grapefruit at nominal rates of 50 g ai/A lb ai/A/application, at 21-day RTIs, for a seasonal rate of 150 g ai/A (equivalent to ~0.33 lb ai/A, 1x the proposed rate). In addition, at one trial location a 2x exaggerated rate (~100 g ai/A/application) was applied. Applications at the 1x rate were made using airblast sprayers in 193-212 gal/A of water with spray oil added at 0.5% v/v.

Samples of 16-48 mature fruit were harvested from each trial 1 day following the last application. Grapefruit were frozen following collection and shipped on dry ice within 1-18 days by overnight courier to the Valent Technical Center, Dublin, CA, where the samples

were stored at ~-20°C. Analyses of pyriproxyfen and 4'-OH-PYR were conducted within 73 days of harvest using method RM-33P-1-3. Residues in all control samples were below the 0.01 ppm LOD for both analytes. Adequate concurrent recoveries were obtained for both compounds. The results are presented in Table 13.

Pyriproxyfen residues were 0.07-0.16 ppm in/on 14 grapefruit samples harvested 1 day after the last of three applications at 1x. At 2x, pyriproxyfen was detected at 0.27 and 0.40 ppm in/on two treated samples. 4'-OH-PYR residues were <0.01 ppm (<LOD) in/on 14 treated samples; from one field trial, residues were 0.01 and 0.02 ppm in/on two samples treated at 1x.

Table 13. Residues of pyriproxyfen and 4'-OH-PYR in/on **grapefruit** harvested following the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at 1x or 2x (nominally 150 g ai or 0.33 lb ai/A total).

Trial Location and Date	Total Appl. Rate (lb ai/A)	PHI	Residues (ppm)	
			Pyriproxyfen	4'-OH-PYR
CA 1996	0.33	1	0.07, 0.11	<0.01, <0.01
CA 1997	0.33	1	0.15, 0.13	<0.01, <0.01
	0.66	1	0.27, 0.40	<0.01, <0.01
CA 1997	0.33	1	0.14, 0.09	<0.01, <0.01
FL 1997	0.33	1	0.13, 0.11	0.01, 0.02
FL 1997	0.33	1	0.14, 0.16	<0.01, <0.01
FL 1997	0.33	1	0.14, 0.13	<0.01, <0.01
TX 1997	0.33	1	0.10, 0.12	<0.01, <0.01

Conclusions: The submitted field trial data on citrus fruits are adequate. Geographic representation of tests on grapefruit, lemons, and oranges conformed to OPPTS Series 860 guidelines and an adequate number of samples was analyzed. Residues of pyriproxyfen were <0.01-0.24 ppm in/on 52 samples of oranges, lemons, and grapefruits treated at 1x. The available data support the proposed tolerance of 0.3 ppm for residues of pyriproxyfen in/on citrus fruit.

Tree Nuts Group

Almonds

Valent submitted data from six field trials conducted in CA during 1997 depicting residues of pyriproxyfen in/on almonds (citation noted below). These data were submitted to support proposed tolerances for residues in/on almond hulls and in/on the tree nuts crop group.

Residue data on walnuts, a member of the tree nut crop group, were previously reviewed by the Agency (PP#7F04882, DP Barcode D238190, W. Donovan, 07-DEC-1998).

MRID 44630102 Pensyl, J. (1998) Magnitude of the Residues of Pyriproxyfen and its Degradates in Almonds: Lab Project Number: VP-11857: TRIAL V-11857-A: TRIAL V-11857-B. Unpublished study prepared by Valent USA Corporation and Excel Research Services, Inc. 519 p. {OPPTS 860.1500}

Pyriproxyfen (0.86 lb/gal EC) was applied three times by broadcast foliar application to almonds at ~0.11 lb ai/A/application, at 14 day RTIs, for a maximum seasonal rate of ~0.33 lb ai/A (1x the proposed rate). In addition, two trials were conducted in which pyriproxyfen was applied three times at ~0.22 lb ai/A/application (~0.33 lb ai/A/season; 2x rate). Application were made using airblast sprayers in 99-103 gal/A of water without the addition of spray adjuvants or oils.

Mature almonds were knocked to the ground 16-21 days after the last application, and the samples were field-dried for 0-5 days according to normal commercial practices. A single control and two treated samples of almonds were collected, husked and shelled, and were stored frozen at the test site for up to 18 days. The samples were then shipped frozen by overnight courier and ACDS freezer truck, or were hand-delivered on ice, to the Valent Technical Center, Dublin, CA where they were stored at ~-20 °C prior to analysis. Samples of nutmeat and hulls were stored frozen for up to 48 and 76 days, respectively, from collection to analysis.

Samples of almond nutmeat and hulls were analyzed for residues of pyriproxyfen and its metabolite, 4'-OH-PYR, using the GC/NPD and HPLC methods RM-33N-2 (nutmeat) and RM-33H (hulls). The LOQ for pyriproxyfen and 4'-OH-PYR in/on each matrix is 0.02 ppm; the LOD for each analyte is 0.01 ppm. Apparent residues of pyriproxyfen and 4'-OH-PYR were <LOD (<0.01 ppm) in/on all control samples of nutmeat and hulls.

Residues of pyriproxyfen were non-detectable (<0.01 ppm) in/on 12 samples of nutmeat. In the studies conducted at 2x the proposed rate, residues of pyriproxyfen were <0.01 ppm in/on three samples of nutmeat, and one sample bore residues at the LOD (0.01 ppm). Residues of 4'-OH-PYR in/on nutmeats were determined for one field trial (Sutter County, CA) and were <0.01 ppm in/on the two nutmeat samples analyzed for this metabolite. Residues of pyriproxyfen and 4'-OH-PYR were 0.26-1.40 ppm and <0.01-0.03 ppm in/on 12 samples of hulls (Table T4). In the two trials conducted at 2x, residues of pyriproxyfen and 4'-OH-PYR were 0.96-3.32 ppm and <0.01-0.04 ppm, respectively, in/on four samples of hulls.

Previously reviewed data are available from four field trials on walnuts conducted in CA during 1996 that were submitted to support a permanent tolerance petition for residues in/on walnuts (PP#7F04882, DP Barcode D238190, W. Donovan, 07-DEC-1998). Walnuts were treated foliarly three times with pyriproxyfen (0.86 lb/gal EC) at ~0.11 lb ai/A/application, at

RTIs of 14 days, for a seasonal application rate of ~0.33 lb ai/A (1x proposed rate). Residues of pyriproxyfen and 4'-OH-PYR were non-detectable (<0.01 ppm) in/on eight walnut samples harvested ~21 days after the last treatment.

Table 14. Residues of pyriproxyfen and 4'-OH-PYR in/on **almond hulls** harvested 16-21 days after the last of three broadcast applications of pyriproxyfen (0.86 lb/gal EC) at the 1x and 2x the proposed rate.

Trial Location by County and State	Total Appl. Rate (lb ai/A)	PHI	Residues (ppm)	
			Pyriproxyfen	4'-OH-PYR
Fresno, CA-1	0.33	16	0.67, 0.69	<0.01, <0.01
Fresno, CA-2	0.33	18	0.73, 0.56	<0.01, <0.01
Madera, CA	0.33	17	1.20, 1.32	0.02, 0.03
	0.66		3.32, 3.20	0.03, 0.04
Butte, CA	0.33	21	1.40, 1.29	<0.01, <0.01
Sutter, CA	0.33	21	0.26, 0.45	<0.01, <0.01
San Joaquin, CA	0.33	21	0.32, 0.44	<0.01, <0.01
	0.66		1.06, 0.96	<0.01, <0.01

Conclusions: The submitted field trial data on almonds are adequate. Residues of pyriproxyfen were non-detectable (<0.01 ppm) in/on 12 samples of nutmeat and 0.26-1.40 ppm in/on 12 samples of hulls harvested 16-21 days following the last of three foliar applications of pyriproxyfen (0.86 lb/gal) at ~0.11 lb ai/A/application (~0.33 lb ai/A/season; 1x the proposed seasonal rate). Residues of pyriproxyfen were <0.02 ppm (<LOQ) and 0.96-3.32 ppm in/on four samples each of nutmeat and hulls treated at 2x the proposed rate.

The available data support the proposed tolerance of 2.0 ppm for residues of pyriproxyfen in/on almond hulls.

The submitted data are inadequate to support the proposed tolerance for residues in/on tree nuts because residue data on the representative commodity pecans were not provided. The petitioner has provided data from a total of 10 field trials, 6 on almonds submitted with this petition, and 4 on walnuts that were previously reviewed, all performed in Region 10. Additional data from 5 trials depicting residues of pyriproxyfen in/on pecans conducted in the Regions specified in OPPTS GLN 860.1500 are required. The trials on pecans should include at least one side-by-side trial using spray oil as an adjuvant.

Alternatively, the petitioner may submit a revised Section F specifying a pyriproxyfen tolerance of 0.2 ppm for almonds.

OPPTS GLN 860.1520: Processed Food/Feed

Oranges

In conjunction with the residue study on oranges (MRID 44630105), the petitioner submitted data depicting residues of pyriproxyfen and 4'-OH-PYR in orange commodities processed from oranges bearing measurable residues. In a field trial conducted in Manatee County, FL, pyriproxyfen (0.86 lb/gal EC) was applied three times foliarly to oranges at 100 g ai/A/application at 21-day RTIs for a total of 300 g ai/A/season (0.66 lb ai/A/season; 2x the proposed rate).

One bulk control and treated sample of oranges (440 lbs each) were harvested 1 day following the last application of pyriproxyfen. On the day of collection, the samples were shipped at ambient temperatures by overnight courier to the processing facility, Englar Food Laboratories, Moses Lake, WA where the samples were processed, within 4 days of collection, into orange fractions using simulated commercial practices, and frozen. The samples were then shipped by overnight courier (on dry ice) to the analytical laboratory, Valent Technical Center, Dublin, CA where the samples were kept at -20°C prior to analysis. The RAC samples and processed orange fractions were analyzed within 7 days of collection.

Residues of pyriproxyfen and 4'-OH-PYR were determined using method RM-33P-1-3. The validated LOQ for each analyte is 0.02 ppm in whole oranges and orange processed fractions. Concurrent method recoveries were adequate. Apparent residues of both analytes were <LOQ (<0.02 ppm) in/on duplicate control samples of each matrix with the exception of control samples of dried pulp which bore residues of 4'-OH-PYR at 0.2 ppm. Residues of pyriproxyfen and 4'-OH-PYR in/on treated samples are presented in Table 15.

Table 15. Residues of pyriproxyfen and 4'-OH-PYR in/on orange commodities processed from oranges harvested 1 day following the last of three foliar applications of pyriproxyfen at 100 g ai/A/application (300 g ai/A or 0.66 lb ai/A total; 2x the proposed rate).

Commodity	Residues (ppm) [a]	Concentration/Reduction factor
Pyriproxyfen		
Whole oranges (RAC)	0.35, 0.35 (0.35)	NA
Oil	25.6, 26.6 (26.1)	74.6x
Pulp, dried	2.17, 2.28 (2.23)	6.4x
Juice	<0.01, <0.01 (<0.01)	0.03x
4'-OH-PYR		
Whole oranges (RAC)	0.02, 0.02 (0.02)	NA

Commodity	Residues (ppm) [a]	Concentration/Reduction factor
Oil	1.2, 1.2 (1.2)	60.0x
Pulp, dried	0.10, 0.12 (0.11)	5.5x
Juice	<0.01, <0.01 (<0.01)	0.5x

[a] Data are duplicate analyses of a single sample for each commodity; average residue values are given in parentheses and used to calculate the concentration factor.

[b] NA = not applicable.

Conclusions: The submitted orange processing study is adequate and indicates that residues of pyriproxyfen do not concentrate in juice, but concentrate by 74.6x in citrus oil and 6.4x in dried pulp. Based upon these concentration factors and the HAFT residues in/on oranges of 0.22 ppm, the proposed tolerances for pyriproxyfen residues in citrus oil and in dried pulp were 20.0 and 1.5 ppm, respectively. **The citrus oil tolerance is appropriate; however, adverse effects disclosure [FIFRA §6(a)(2)] data from California indicates that a citrus dried pulp tolerance of 2.0 ppm is needed.**

Tomato

Valent submitted data depicting the potential for concentration of pyriproxyfen residues in the processed commodities of tomatoes. The data were included in the submission of field trial data (MRID 44630103).

One bulk control and treated sample of tomatoes (150 lbs) were harvested 14 days following three treatments totaling 5x the maximum proposed rate from a trial conducted in CA. The samples were shipped on the day of harvest to Wm. J. Englar and Associates, Moses Lake, WA. Tomatoes were processed using simulated industrial procedures into tomato puree and paste. The samples were returned to Valent and stored at -20°C until analysis using method RM-33P-8, described above. Pyriproxyfen and PYPA were determined using the methods for tomatoes described previously.

Conclusions: This tomato processing study is adequate. Pyriproxyfen residues were 0.04 ppm in whole tomatoes, 0.02 ppm in paste, and <0.01 ppm in puree. As there was no concentration, separate tolerances for tomato paste and puree are not required.

OPPTS GLN 860.1480: Meat, Milk, Poultry and Eggs

An adequate cattle feeding study has been previously reviewed (PP#7F04882, DP Barcode D238190, W. Donovan, 07-DEC-1998), and the Agency concluded that tolerances would not be required for residues of pyriproxyfen in animal commodities provided that no additional

uses on livestock feed items are proposed. The maximum theoretical dietary burden (MTDB) for beef and dairy cattle was calculated at 1.69 and 1.29 ppm, respectively, using estimated tolerances for almond hulls (2.0 ppm), apple wet pomace (0.8 ppm), dried citrus pulp (1.0 ppm), cottonseed (0.05 ppm) and cotton gin byproducts (2.0 ppm).

Based on the data submitted with the current petition, the calculated MTDB (Table 16) for beef and dairy cattle has increased slightly to 1.91 and 1.51 ppm, respectively, based on a more appropriate tolerance of 2.0 ppm for pyriproxyfen residues in dried citrus pulp (D253882, W. Donovan, 22-MAR-1999). This adjustment does not significantly affect the maximum expected dietary burden of pyriproxyfen residues for livestock.

There are no poultry feed items associated with this petition. Therefore, no additional secondary residues are expected to occur in poultry eggs, fat, meat, and meat byproducts as a result of the proposed uses. In conjunction with the petition for use on cotton (PP#6F4737, DP Barcodes D228556, D228925, and D228926, J. Garbus, 06-MAY-1997), the Agency concluded that secondary residues in poultry and eggs are unlikely in light of the poultry metabolism study results.

Table 16. Calculation of the maximum theoretical dietary burden of pyriproxyfen in beef and dairy cattle.

Feed Commodity	Estimated Tolerance (ppm)	% Dry Matter [a]	Beef Cattle		Dairy Cattle	
			% of Diet	Burden, ppm	% of Diet	Burden, ppm
Apple, pomace, wet	0.8 [b]	40	40	0.80	20	0.40
Cotton gin byproducts	2.0 [c]	90	20	0.44	20	0.44
Citrus, pulp	2.0	91	20	0.44	20	0.44
Almond hulls	2.0	90	10	0.22	10	0.22
Cotton, seed	0.05 [c]	88	10	0.01	25	0.01
TOTAL			100	1.91	95	1.51

[a] Table 1, OPPTS GLN 860.1000.
[b] Based on apple residue data (PP#7F04882, DP Barcode D238190, W. Donovan, 07-DEC-1998).
[c] Based on cotton residue data (PP#6F4737, DP Barcodes D228556, D228925, and D228926, J. Garbus, 06-MAY-1997).

Conclusions: Typically, tolerances are required on all animal commodities having detectable residue levels at a 10x dosing rate or below. For the computed MTDB of 1.91 ppm in beef cattle, this would include the 3 and 9 ppm dosing levels. The only commodity having detectable pyriproxyfen residues at these levels was fat: 0.01 - 0.03 ppm. Since the MTDB calculation is based on a nutritionally unbalanced diet and includes contributions from some animal feed items that are used only regionally, HED will not require the establishment of pyriproxyfen tolerances in fat at this time. However, should future new uses include additional animal feed items, tolerances on animal commodities will be needed.

OPPTS GLNs 860.1850 and 860.1900: Confined/Field Accumulation in Rotational Crops

No rotational crop studies are required for citrus or tree nuts (Residue Chemistry Test Guidelines,OPPTS 860.1850). An adequate confined rotational crop study (MRID 44036918) was conducted in support of the cotton petition (PP#6F4737, DP Barcodes D228556, D228925, and D228926, J. Garbus, 06-MAY-1997). Based on a 30-day plantback interval and a treatment rate of 0.18 lb a.i./A, no pyriproxyfen residues above 0.01 ppm were found in any of the following crop matrices: lettuce leaf; radish tops and roots; and wheat grain, forage, straw and chaff. **Accordingly, HED concludes that a 30-day plantback interval for rotational crops is needed for fruiting vegetables when treated with pyriproxyfen as directed.**

Note to RD: The pyriproxyfen cotton label should also be amended to specify a 30-day plantback interval for rotational crops.

Codex Harmonization

An International Residue Limits Status sheet is attached. There are no Codex, Canadian, or Mexican tolerances for residues of pyriproxyfen in/on almonds, citrus fruits, or fruiting vegetables; thus, harmonization is not an issue. Pyriproxyfen is scheduled as a new compound for JMPR review (both toxicology and chemistry) in 1999.

Attachment 1: EPA memoranda cited in this review.
Attachment 2: International Residue Limit Status sheet for pyriproxyfen.
Attachment 3: Pyriproxyfen and its metabolites in tomatoes.

cc with Attachments: PP#8F05022, RAB1 File, W.H. Donovan, O. Odiott
RDI: G. Kramer (22-MAR-1999), RAB1 Chemists (19-MAR-1999), M. Morrow (25-MAR-1999)
W. Donovan:CM#2:RM804E:305-7330:25-MAR-1999

Attachment 1

EPA MEMORANDA CITED IN THIS REVIEW

DP Barcode:	D228395
Subject:	Residues of Concern for Pyriproxyfen in Plants. Results of the HED Metabolism Committee Meeting Held on 15-JUL-1996.
From:	R. Loranger
To:	The HED Metabolism Committee
Dated:	10-SEP-1996
MRID(s):	None

CBTS No.:	17440
DP Barcode:	D228556, D228925, and D228926
Subject:	PP#6F4737. Pyriproxyfen on Cotton. Evaluation of Analytical Methods, Field Trial, and Processing Residue Data.
From:	J. Garbus
To:	K. Boyle
Dated:	06-MAY-1997
MRID(s):	44036901-44036904, 44036918-44036920, 44036922-44036930, 44037201, and 4437204.

DP Barcode:	D241303, D228499
Subject:	PP#6F04737. Pyriproxyfen on cotton. HED Risk Assessment.
From:	W. Donovan, W. Dykstra, B. Tarplee
To:	S. Lewis, J. Tavano
Dated:	27-FEB-1998
MRID:	None

DP Barcode:	D250953
Subject:	Pyriproxyfen. Results of the Metabolism Assessment Review committee Meeting Held on 10-NOV-1998.
From:	W. Donovan, W. Dykstra
To:	G. Kramer
Dated:	19-NOV-1998
MRID:	None

DP Barcode:	D238190
Subject:	PP#7F04882. Pyriproxyfen in/on Pome Fruits and Walnuts. Evaluation of Residue Data and Analytical Methods.
From:	W. Donovan
To:	S. Lewis/J. Tavano
Dated:	07-DEC-1998

MRID: 443295-05 through -12

DP Barcode: D252371
Subject: PP#s 7F04882 and 8F05022. Pyriproxyfen in/on Citrus Fruits, Pome Fruits, Fruiting Vegetables, and Tree Nuts. Request for Petition Method Validation (PMV).
From: W. Donovan
To: D. Marlow
Dated: 28-JAN-1999
MRID: None

DP Barcode: D253882
Subject: ID#99CA0011. Pyriproxyfen in/on Citrus Pulp, Dried. Review of Temporary Tolerance Level Based on Data Submitted Under FIFRA §6(a)(2).
From: W. Donovan
To: A. Beard and R. Forrest
Dated: 22-MAR-1999
MRID: None

Attachment 2

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name:	Common Name: pyriproxyfen	X☐ Proposed tolerance ☐ Reevaluated tolerance ☐ Other	Date: 15-JAN-1999

Codex Status (Maximum Residue Limits)	U. S. Tolerances
X☐ No Codex proposal step 6 or above ☐ No Codex proposal step 6 or above for the crops requested	Petition Number: 8F05022 DP Barcode: Other Identifier:
Residue definition (step 8/CXL): N/A	Reviewer/Branch: W. Donovan/RAB1
	Residue definition: pyriproxyfen

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Citrus fruits	0.3 ppm
		Fruiting Vegetables	0.1 ppm
		Tree Nuts	0.02 ppm
		Almond, hulls	2.0 ppm
		Citrus, oil	20.0 ppm
		Citrus, pulp, dried	1.5 ppm

Limits for Canada	Limits for Mexico
X☐ No Limits ☐ No Limits for the crops requested	X☐ No Limits ☐ No Limits for the crops requested
Residue definition: N/A	Residue definition: N/A

Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions: Codex, Scheduled as a new chemical in 1999 (tox and residue)

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Attachment 3

Figure 1. Pyriproxyfen and its metabolites in tomatoes.

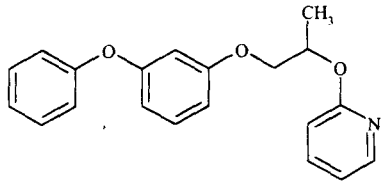
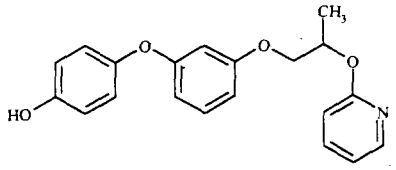
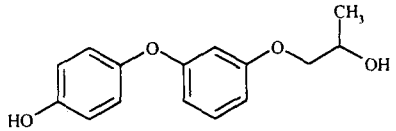
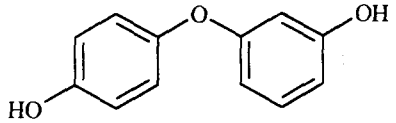
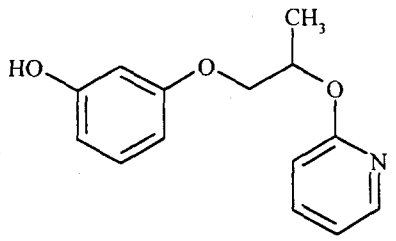
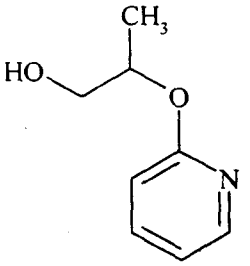
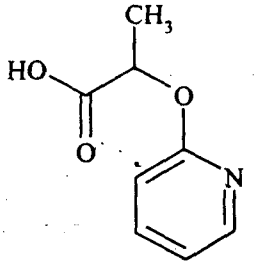
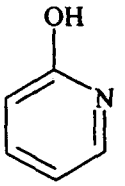
Common Name Chemical Name	Structure	Substrate
Pyriproxyfen 4-phenoxyphenyl (*RS*)-2-(2-pyridyloxy)propyl ether		Phenyl- and pyridyl-labeled tomato
4'-OH-PYR 4-(4-hydroxyphenoxy)phenyl (*RS*)-2-(2-pyridyloxy)propyl ether		Phenyl- and pyridyl-labeled tomato
4'-OH-POPA 4-(4-hydroxyphenoxy)phenyl (*RS*)-hydroxypropyl ether		Phenyl-labeled tomato
4'-OH-POP 4,4-oxydiphenol		Phenyl-labeled tomato
DPH-PYR 4-hydroxyphenyl (*RS*)-2-(2-pyridyloxy)propyl ether		Phenyl- and pyridyl-labeled tomato

Figure 1. (continued).

Common Name Chemical Name	Structure	Substrate
PYPA (*RS*)-2-(2-pyridyloxy)propyl alcohol		Pyridyl-labeled tomato
PYPAC (*RS*)-2-(2-pyridyloxy)propionic acid		Pyridyl-labeled tomato
2-OH-PY 2-hydroxypyridine		Pyridyl-labeled tomato